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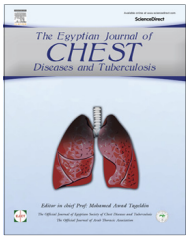

ORIGINAL ARTICLE

Role of IOS in evaluation of patients with interstitial lung diseases

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KEYWORDS

IOS;
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Abstract *Aim:* In patients with ILD, a static expiratory pressure–volume curve of the lung is generally shifted downward and rightward and spirometry results reveal reduced vital capacity (Thompson et al., 1989). However, reduced vital capacity may occur even in patients with obstructive lung diseases and in other situations, such as chest wall restriction, lung resection, inspiratory muscle weakness, or poor cooperation with spirometry. In addition, spirometry is sometimes difficult to perform with elderly, cognitively impaired patients, or severe respiratory distress (Kubota et al., 2009). IOS is a simple, noninvasive method requiring only passive patient cooperation that allows for the evaluation of lung function through the measurement of both airway resistance and airway reactance. The aim of this study is to assess the role of IOS in the evaluation of the cases of interstitial lung diseases.

Methodology: This study included 48 patients with interstitial lung diseases of different causes. Pulmonary function test by spirometry was done to measure FEV1, FVC, FEV1/FVC, MEF25-75 and pulmonary function test by impulse oscillometry (IOS). We measured R5, R20, X5, RF. Oxygen saturation and 6MWT.

Results: In our study 87% were females. The mean age in our study was 50.75 ± 11.1. Mean X5 was low in ILD denoting restrictive pattern, and there was a negative correlation between X5 and FEV1/FVC. There was a positive correlation between X5 and 6MWT. The mean R5 was 150.33 ± while mean R20 was 108.33 ± 48.66 this is within normal then this is considered an index of mild small airways obstruction.

Introduction

Pulmonary function testing is used to evaluate respiratory mechanics and physiology in both children and adults with suspected respiratory diseases. Spirometry is perhaps the most commonly used pulmonary function test with the advantage of being readily available in both inpatient and outpatient settings, including many primary care offices. Lung volume

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measurement by body plethysmography or gas dilution requires more-expensive equipment that often requires a dedicated pulmonary function testing laboratory. Simple spirometry and body plethysmography often can be performed successfully in children but may be limited by the child's ability to follow directions and provide maximal, reproducible efforts. Some of the challenges in performing spirometry in younger children, especially those aged 2–5 years, may have led to this diagnostic modality being significantly underused. Current data suggest that only 21% of primary care practitioners use spirometry in the diagnosis of asthma in children [1].

Interstitial lung diseases alter mechanical and gas exchange properties of the lungs. In general, the hallmarks of interstitial lung diseases are restrictive changes in pulmonary physiology (i.e., reduced total lung capacity, reduced residual volume, decreased static compliance, and a reduced VC, often with an increased FEV1/FVC ratio), and a reduced diffusing capacity for carbon monoxide (DlCO). A few diseases also manifest substantial components of airflow obstruction [2].

In patients with ILD, a static expiratory pressure–volume curve of the lung is generally shifted downward and rightward and spirometry results reveal reduced vital capacity [3]. However, reduced vital capacity may occur even in patients with obstructive lung diseases and in other situations, such as chest wall restriction, lung resection, inspiratory muscle weakness, or poor cooperation with spirometry. In addition, spirometry is sometimes difficult to perform with elderly, cognitively impaired patients, or patients with severe respiratory distress [4].

The forced oscillation technique is the general name for airway mechanic measurements using the noninvasive superimposition of pressure fluctuations on the airway over the subject's normal, quiet, tidal breathing. More than 50 years ago, FOT was first determined by Dubois et al. [5] and has developed with regard to configuration, standardization, and application. Impulse oscillometry is one type of FOT. Other techniques of FOT use only one frequency or change the frequency "pseudo randomly". Impulse oscillometry delivers a regular square wave of pressure 5 times per second, which has the advantage of generating a larger sample during measurements and emitting a continuous spectrum of frequencies that may provide a more detailed characterization of respiratory function [6]. Impulse oscillometry has been used in adults as well as in preschool children to identify lung dysfunction, such as in asthma [7].

IOS is a simple, noninvasive method requiring only passive patient cooperation that allows for the evaluation of lung function through the measurement of both airway resistance and airway reactance [1]. Current IOS procedures are based on the physiologic concepts of the forced oscillation technique originally described by Dubois et al. [5] in 1956. IOS uses sound waves to rapidly detect airway changes and requires only normal tidal breathing from the patient [1].

The main advantage of FOT/IOS is that the patient needs to perform simple tidal breathing maneuvers that require less effort and co-operation than spirometry, meaning that children and the elderly can therefore perform this test easily. Moreover, it can be performed in patients on ventilators and also during sleep. One of the most remarkable features of FOT/IOS in relation to spirometry is that it has much greater sensitivity to detect peripheral airways obstruction. In most cases, spirometry does not provide a clear indication of peripheral airway obstruction regardless of the information contained in the flow–volume curve and the forced expiratory flow at 25–75% of forced vital capacity ($FEF_{25–75\%}$). FOT/IOS are therefore more sensitive instruments to detect small airway obstruction in patients with asthma and chronic obstructive pulmonary disease (COPD). More recently, the within-breath analysis of R_{rs} and X_{rs} has been shown to help differentiate between asthma and COPD and also offer more useful information about the pathophysiology of asthma and COPD, which the spirometer does not [8].

IOS is well suited for conditions involving airway obstruction, but it may not provide definitive information on restrictive states [9] although more research into this area is needed [1].

Two components of respiratory impedance can be evaluated by forced oscillometry: total respiratory resistance and reactance [10]. Resistance at low frequency, 5 Hz (R5), indicates total airway resistance and resistance at high frequency, 20 Hz (R20), approximates central airway resistance. The difference between R5 and R20 (R5 − R20) is considered to be an index of the small airways [11]. Reactance at 5 Hz (X5) is thought to be reciprocally related to compliance. The resonant frequency (Fres) is the intermediate frequency at which the total reactance is 0, and reactance area (AX) is the integrated low frequency respiratory reactance magnitude (area under the curve) between 5 Hz and Fres [12]. X5, Fres, and AX have been proposed for detecting expiratory flow limitations [13–15].

Interpretation of IOS

R5 total respiratory Resistance – abnormal, if above 150% predicted
X5 distal capacitive Reactance – abnormal, if below X5 predicted – 0,15 kPa/(l/s)

Lung function is abnormal, if either R5 or X5 or both parameters are within the abnormal range. R5 and X5 are invoked together for the determination of the degree of severity of disease [15].

in [kPa/(l/s)]	X5 predicted – 0,15	⩾X5> X5 Predicted – 0,3	⩾X5> X5 Predicted – 0,6	X5 predicted-0,6
R5 < 150% predicted	Normal	I (slight)	II (moderate)	III (severe)
150% ⩽ R5 < 200% predicted	I (slight)	II (moderate)	III (severe)	III (severe)
200% ⩽ R5 < 300% predicted	II (moderate)	III (severe)	III (severe)	III (severe)
R5 ⩾ 300% predicted	III (severe)	III (severe)	III (severe)	III (severe)

Aim of the study

The aim of this study is to evaluate the role of IOS in assessment of the cases of interstitial lung diseases as simple technique that requires less patient cooperation since those patients are usually dyspneic and may not be cooperative.

Methodology

This study was conducted in the pulmonary function unit at the chest department, Kasr Elaini hospital, in the period August 2015 to March 2016. It included 48 patients with interstitial lung diseases.

Inclusion criteria: 1-Diagnosed patients of interstitial lung disease.

Exclusion criteria:

1. Any other chest diseases eg COPD, Asthma, Bronchogenic carcinoma... etc
2. Cardiac patients.

The following was performed to each patient:

1. Proper history taking and full clinical examination.
2. Routine laboratory examination including CBC, ESR, Kidney and liver function tests.
3. Measuring oxygen saturation by pulse oximetry and performing 6 MWT.
4. Collagen profile.
5. High resolution CT chest.
6. Some patients were subjected to TBLB or thoracoscopic lung biopsy for diagnosis.
7. Pulmonary function test by spirometry to measure FEV1, FVC, FEV1/FVC, and MEF25-75
8. Pulmonary function test by impulse oscillometry (IOS) by device Master Screen IOS Carefusion Germany 234GmbH Leibnizstrasse 7 D-97204 Hoechberg SN 737390 IP 20

We measured R5, R20, X5, and RF.

N.B. some patients performed the IOS test were not able to do spirometry because of their dyspnea were excluded from this study.

Table 1 Sex distribution of the patients.

	No	Percentage
Male	6	12.5
Female	42	87.5
Total	48	100

Results and Discussion

In our study it was female dominant as shown in Table 1 were 87% were females which was the same in another study done by Risa Sokai, Satoru Ito, et al. [16] but in their study they were considering only patients with RA., while in another study done by A. Sugiyama [17] males were more than females in the group of ILD included in their study.

Table 2 shows that more than one third of our cases were cases of ILD secondary to Rheumatoid arthritis followed by cases of non specific interstitial pneumonitis (NSIP) the lower percentages were those of hypersensitivity pneumonitis (HP), sarcoidosis and scleroderma.

The mean age in our study was 50.75 ± 11.13 as shown in Table 3 which matches with the results of the study done by Elena Semenova [18] 54.46 ± 9.9 year, while the mean age of ILD patients in the study done by A. Sugiama et al. [17] was age 65.8 ± 0.9 years.

Table 5 in this study shows a decreased X5 in patients with ILD which is matching with the study done by A. Sugiama et al. [17] where the mean X5 was −0.19 ± 0.01 whereas in our study the mean X5 was – 0.20.

In this study Table 5 shows mean R5 (which refers to small and large airways) was 150.33 ± which is a mild degree of obstruction while mean R20 (which refers to large airways only) was 108.33 ± 48.66 this is within normal then this is considered an index of small airways obstruction this result was similar to the results obtained by spirometry in Table 4 that shows that mean MEF25-75 was 55.25 ± 18.11 that denotes small airway obstruction too.

Table 3 Minimum, maximum, mean and St deviation results of the Age, O2 saturation and 6MWT.

	Min	Max	Mean	St deviation
Age	29.00	73.00	50.79	11.13
O2 Sat	80.00	98.00	93.04	5.06
6MWT	100.00	355.00	251.50	76.48

Table 4 Descriptive statistics of the results of the spirometry study.

	Minimum	Maximum	Mean	Std. Deviation
FEV1/FVC	80.00	100.00	88.7917	6.12618
FVC%	22.00	78.00	56.2917	15.33867
FEV1%	24.00	80.00	57.3750	14.74554
MEF25-75	24.00	100.00	55.2500	18.11371

Table 2 Diagnosis varieties that were included in this study.

	RA-ILD	Scleroderma	HP	Sarcoidosis	NSIP	IPF	Total
No	16	2	6	4	12	8	48
%	33.4	4.2	12.5	8.2	25	16.7	100

Table 5 Descriptive statistics of the results of the IOS study.

	Min	Max	Mean	St deviation
R5%	60.00	306.00	150.3333	64.64085
R20%	46.00	226.00	108.3292	45.66735
X5act	−.42	−.07	−.2029	.09406
AAx	.12	6.45	2.2271	1.65970
RRf	17.30	29.00	23.4750	3.89569

Table 6 Comparison between categorization of the restriction degree between spirometry and IOS.

	Spirometry	IOS
Normal		16
Mild	20	28
Moderate	22	4
Severe	6	

Table 8 Comparison between spirometry and IOS in correlation to O2 saturation.

	Spirometry O2 sat (Mean ± SD)	IOS O2 sat(Mean ± SD)
Normal		94.7 ± 2.3
Mild	96.5 ± 1.7	91.6 ± 6
Moderate	91.0 ± 4.5	96.5 ± 0.5
Severe	89.0 ± 7.6	

Table 9 Comparison between spirometry and IOS in correlation to 6MWT.

	Spirometry restriction 6MWT Mean ± SD	IOS restriction 6MWT Mean ± SD
Normal		261.3 ± 57.6
Mild	289.6 ± 72.6	247.4 ± 80.1
Moderate	245.9 ± 53.4	241.0 ± 28.1
Severe	145.0 ± 58.5	

In another study [16] on patients with rheumatoid arthritis with ILD there were Rrs values significantly higher during the expiratory phase than during the inspiratory phase ($P < 0.001$) at most frequencies Xrs values during a whole breath, inspiration, and expiration were also significantly increased as a function of frequency in our study 33.4% of our patients was secondary to RA (see Table 6).

In this study there is a negative correlation between X5 and FEV1/FVC as shown in Table 7 but it was not statistically significant which matches with the restrictive pattern this supports the conclusion in the study done by A. Sugiyama [17] that suggested that ΔX5 is a characteristic feature of IOS measurements in ILD patients, which is clearly different from those in asthma and COPD patients. This within-breath X5 change in ILD might be associated with its severity and physiological abnormality. Also our study showed negative correlation between X5 and FEV1 which is similar to the study done by Elena Semenova [18] Correlation analysis showed a

Table 7 Correlations between different spirometry measured items and IOS measured items.

			FEV1/FVC	FVC %	FEV1%	R 5%	MEF25-75%	R 20%	X5 act	O2 SAT %
Spearman's rho	FEV1/FVC	Correlation Coefficient	1.000	−.515	−.279	−.078	.305	.108	−.096	−.508
		Sig. (2-tailed)	.	.000	.055	.599	.035	.467	.516	.000
	FVC%	Correlation Coefficient	−.515	1.000	.912	.114	.101	−.220	.201	.654
		Sig. (2-tailed)	.000	.	.000	.438	.493	.134	.171	.000
	FEV1%	Correlation Coefficient	−.279	.912	1.000	.236	.299	−.122	.008	.639
		Sig. (2-tailed)	.055	.000	.	.106	.039	.407	.955	.000
	R 5%	Correlation Coefficient	−.078	.114	.236	1.000	.093	.738	−.474	.159
		Sig. (2-tailed)	.599	.438	.106	.	.527	.000	.001	.281
	MEF25-75%	Correlation Coefficient	.305	.101	.299	.093	1.000	.259	−.043	−.033
		Sig. (2-tailed)	.035	.493	.039	.527	.	.076	.770	.823
	R 20%	Correlation Coefficient	.108	−.220	−.122	.738	.259	1.000	−.302	−.090
		Sig. (2-tailed)	.467	.134	.407	.000	.076	.	.037	.542
	X5 act	Correlation Coefficient	−.096	.201	.008	−.474	−.043	−.302	1.000	.021
		Sig. (2-tailed)	.516	.171	.955	.001	.770	.037	.	.887
	O2 SAT%	Correlation Coefficient	−.508	.654	.639	.159	−.033	−090	.021	1.000
		Sig. (2-tailed)	.000	.000	.000	.281	.823	.542	.887	.

Highly correlated R20 positive X5 neg.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

significant negative correlation between ΔX5 and TLC, VC, RV, and FEV1.

In 1968, Fisher et al. [19] showed evidence of increased respiratory resistance on FOT in patients with ILD, but the sample size was small and the FOT analysis was only very basic. In 2009, van Noord et al. [20] reported increased R_{rs} and reduced X_{rs} in patients with advanced ILD, but these values were similar to those observed in patients with moderate-to-severe COPD. The authors therefore commented that the results of FOT cannot help differentiate between obstructive and restrictive disorders.

In 2013, Mori et al. [21] reported that although the total X_5 values were lower in ILD and comparable to patients with COPD, the X_5 values were smaller in the expiratory phases compared with the inspiratory phases in ILD, which is the reverse of what is found in patients with COPD.

Table 7 shows negative correlation between X5 and FEV1/FVC. In our study Table 8 showed that there was no correlation between the result of the IOS degree of X5 limitation and the oxygen saturation of the patients on room air, this point needs more research to find an explanation.

Table 9 shows that the more the degree of restriction as referred to by the X5 value the lower the distance of 6MWT but there were no statistically significant correlations these results were the same found by the spirometry test.

Conclusions and recommendations

1. X5 was lower in patients with ILD that denotes restrictive pattern.
2. There is negative correlation between X5 and FEV1/FVC.
3. There was a positive correlation between X5 and 6MWT.
4. Mean R5 was mildly impaired mean R20 was within normal denoting small airway obstruction.
5. IOS test was easier to be performed and needed less patient cooperation whatever the degree of severity of the ILD disease.
6. Correlation between X5 and oxygen saturation.
7. The IOS and spirometry should not replace each other in the follow up of the same patient as the degree of the disease was not the same by both tests.
8. Spirometry is currently more widely adopted and better studied therefore, interpretation of its results often are more straight forward to the practitioner yet more studies are needed on ILD by IOS to encourage its use.

Conflict of interest

There is no conflict of interest in this study.

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